DETAILED ACTION

This application is in response to Applicant's amendment filed October 26, 2011. Claims 1-12 and 15-16 are pending in the application. Claims 2, 8, 12, and 15-16 have been amended. Claims 3, 5-6, and 10-12 are withdrawn from consideration as being drawn to a non-elected invention and species. Claims 1-2, 4, 7-9, and 15-16 will presently be examined to the extent they read on the elected subject matter of record.

Status of the Claims

Rejections not reiterated from the previous Office Action are hereby withdrawn. The following rejections are reiterated. They constitute the complete set of rejections presently being applied to the instant application.

The rejection of claims 1-2, 4, and 15-16 under 35 U.S.C. 102(b) as being anticipated by the Feng Publication (1998) (Feng et al.) **is maintained**.

The rejection of claims 1-2, 4, and 15-16 under 35 U.S.C. 102(b) as being anticipated by the King et al. (US 6,339,075) **is maintained**.

The rejection of claims 1-2, 4, 7-9, and 15-16 under 35 U.S.C. 102(b) as being anticipated by the Edwards et al. (CA 2,483,917) **is maintained**.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4, and 15-16 are rejected under 35 U.S.C. 102(b) as being anticipated by the Feng Publication (1998) (Feng et al.).

Feng et al. disclose that most patients with cystic fibrosis (CF) are infected with *Pseudomonas aeruginosa*. Feng et al. disclose that dextran exhibits antiadhesive effects in preventing attachment of *P. aeruginosa* to epithelial cells (epithelial protection). Feng et al. disclose that the initial purpose of the study was to evaluate the potential of dextran to alter the rheology and ciliary transportability of CF sputum prior to initiation of a clinical trial in patients with CF. Feng et al. disclose that overall, whether for CF sputum or healthy dog mucus, Dextran 4000 treatment significantly reduced viscoelasticity and increased predicted mucociliary and cough clearability (enhancing mucus function administering a mucothickening agent, dextran). Feng et al. further disclose that treatment with Dextran 4000 can reduce the crosslink density and cohesiveness of CF and improve mucociliary and cough clearability . Dextran 4000 is an inexpensive and nontoxic agent that may be of benefit in patients with CF lung disease and perhaps in other respiratory disease where mucus retention is an important feature (Abstract).

Feng et al. meet all the limitations of the claims and thereby anticipate the claims.

Claims 1-2, 4, and 15-16 are rejected under 35 U.S.C. 102(b) as being anticipated by the King et al. (US 6,339,075).

King et al. disclose a method of improving mucus clearance comprising administering to the respiratory tract of a patient in need of such treatment an effective

amount of a polysaccharide (col. 2, lines 57-60) (method of enhancing mucus function comprising administering an effective amount of a mucothickening agent, polysaccharide). King et al. disclose a method of improving mucus clearability in a patient having cystic fibrosis comprising administering to the respiratory tract of the patient in need of such treatment an effective amount of dextran (col. 2, lines 66-67-col. 3, lines 1-3) (dextrin, respiratory lining). King et al. disclose that the mechanism for the improvement in viscoelasticity with dextran administration is believed to be due to the substitution of dextran moieties in hydrogen bonding sites otherwise occupied by oligosaccharide moieties linked to neighboring high molecular weight peptides. The original intermolecular mucin-mucin bonds contribute to the three-dimensional structure that makes up the mucus gel, while the new mucin-dextrin bonds form ineffective crosslinks because of the relatively small length of the dextran polymer (col. 4, lines 16-25).

King et al. meet all the limitations of the claims and thereby anticipate the claims.

Response to Arguments

Applicant's arguments filed October 26, 2011 have been fully considered but they are not persuasive. Applicant argues that both Feng et al. and King et al. disclose the use of Dextran 4000, a low molecular weight dextran. Applicant argues that Dextran 4000 is a low molecular weight dextran and would be understood by person skilled in the art to be a mucolytic agent since it serves to reduce mucin gel crosslinking by disrupting intermolecular mucin-mucin H bond crosslinks. Applicant argues that breaking covalent bonds with mucolytic agents reduces mucin molecular weight and

results in decreased mucus viscoelasticity and that on the contrary, the mucothickening agents of the present invention do the opposite. Applicant argues that the mucothickening agents of the present invention promote the formation of one or more covalent bonds, ionic bonds, hydrogen bonds, van der Waals' force, etc. in the mucus. The mucothickening agents of the present invention reduce the aerosolizability of respiratory secretions while maintaining mucociliary clearability, and thus normal airway clearance function. In response to Applicant's argument, Applicant claims a method of enhancing mucus function which comprises administering an effective amount of a mucothickening agent to a subject in need thereof. Applicant claims that enhancing of mucus function is improving physical and/or biochemical properties of the layer of mucus lining the respiratory system. Applicant further claims in claim 15 that the mucothickening agent is selected from the group consisting of dextran. Applicant is not specific as to the type of dextran that can be used as the mucothickening agent. Feng et al. teach that the use of dextran 4000 reduces the viscoelastic modulus of CF sputum, which leads to a substantial increase of sputum cough clearability. Therefore, based on a broad interpretation of the claims the skilled artisan would recognize that the use of dextran 4000, which is the same compound claimed, dextran, would improve the physical and/or biochemical properties of the layer of mucus lining the respiratory system. The improvement that is exhibited by dextran 4000 in the teachings of Feng et al. is a reduction in the crosslink density and cohesiveness of CF and improve mucociliary and cough clearability. The improvement exhibited by dextran 4000 in the teachings of King et al. is improved mucus clearability in a patient. Therefore, the skilled

artisan would expect that dextran 4000 being one of the compounds claimed would also have the properties of formation of one or more covalent bonds, ionic bonds, hydrogen bonds, van der Waals' force, etc. in the mucus.

Applicant argues that in an embodiment of the present invention, the mucothickening agent is HMW dextran. The HMW dextran has approximately the same molecular weight as the subunits of mucin macromolecules; in this case mucin-dextrin crosslinks are approximately as effective as the original mucin-mucin crosslinks. HMW raises elasticity relative to viscosity, thus its use would tend to inhibit aerosolizability, which depend on spinnability, while maintaining mucociliary clearability. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., HMW dextran) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant claims in claim 15 that the mucothickening agent is selected from the group consisting of dextran. Applicant is not specific as to the type of dextran that can be used as the mucothickening agent, LMW or HMW dextran.

Claims 1-2, 4, 7-9, and 15-16 are rejected under 35 U.S.C. 102(b) as being anticipated by the Edwards et al. (CA 2,483,917).

Edwards et al. disclose that formulations have been developed for pulmonary delivery to treat or reduce the infectivity of diseases such as viral infections, especially

tuberculosis, SARS, influenza, cytomegalovirus and RSV in humans and hoof and mouth disease in animals. Edwards et al. disclose the formulations for pulmonary administration include a material that significantly alters physical properties, such as surface tension, surface elasticity and bulk elasticity of lung mucus lining fluid, which may be a surfactant and optionally, a carrier. The formulation may be administered as a powder where the particles consist basically of the material altering surface properties, such as surface tension and/or surface and/or bulk elasticity. The carrier may be a solution, such as alcohol, or a material mixed with the material altering surface properties to form particles. Edwards et al. disclose these include polysaccharides such as dextran, which also has surface active properties (page 7, lines 5-16). Edwards et al. disclose the formulations are administered either as a powder or aerosol, preferably prior to or shortly after infection, to decrease or prevent infection and then viral shedding. Edwards et al. disclose the formulation is administered in an amount sufficient to decrease surface instabilities in the liquid lining the airways of the lung, i.e., to damp the rate of droplet formation from lung fluid (page 7, lines 22-30). Edwards et al. disclose that an example shows using a suitable quantity and size of a macromolecule, such as 50 K Da dextran can also significantly reduce aerosolization (decreasing aerosolization).

Edwards et al. meet all the limitations of the claims and thereby anticipate the claims.

Response to Arguments

Applicant's arguments filed October 26, 2011 have been fully considered but they are not persuasive. Applicant argues that 50K Da dextran is a low molecular weight dextran and that this would not be considered by persons skilled in the art to be a mucothickening agent. In response to Applicant's argument, Applicant claims a method of enhancing mucus function which comprises administering an effective amount of a mucothickening agent to a subject in need thereof. Applicant claims that enhancing of mucus function is improving physical and/or biochemical properties of the layer of mucus lining the respiratory system. Applicant further claims in claim 15 that the mucothickening agent is selected from the group consisting of dextran. Applicant is not specific as to the type of dextran that can be used as the mucothickening agent. Edwards et al. disclose the formulations for pulmonary administration include a material that significantly alters physical properties, such as surface tension, surface elasticity and bulk elasticity of lung mucus lining fluid, which may be a surfactant and optionally, a carrier. Edwards et al. disclose these include polysaccharides such as dextran, which also has surface active properties. Edwards et al. further disclose the formulations decrease or prevent infection and then viral shedding. Edwards specifically teaches that 50K Da dextran leads to less aerosol emitting from lung fluids if administered in appropriate amounts and appropriate frequencies. Therefore, the skilled artisan would interpret decreased or less aerosol emission as decreasing aerosolizable respiratory secretions.

Applicant argues that Edwards et al. teaches in one example that a solution comprising 500K Da dextran would not be considered a mucothickening agent because it resulted in an increase in fluorescence reaching the filter, which indicates that the use of this solution dramatically leads to greater aerosol emission, an undesirable result in a method for limiting infectivity and transmission of airborne diseases. In response to Applicant's argument, the use of the 500K Da dextran is a single embodiment disclosed in the teachings of Edwards. The teaching of Edwards et al. should be taken as a whole, which also teaches that compositions that contain dextran, particularly 50K Da dextran leads to less aerosol emitting from lung fluids if administered in appropriate amounts and appropriate frequencies. Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). “A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use.” In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). Applicant states that HMW dextran means mean molecular weight ca. 70,000 Daltons or greater, more suitably in the range of 100,000-1,000,000 Daltons. Applicant further states that the HMW dextran has approximately the same molecular weight as the subunits of mucin macromolecules; in this case mucin-dextran crosslinks are approximately as effective as the original mucin-mucin crosslinks. HMW dextran raises elasticity relative to viscosity, thus its use would tend to inhibit aerosolizability, which will depend on spinnability, while maintaining mucociliary clearability. The examiner notes that the formulation comprising the 500K

Da dextrin falls within Applicant's definition of HMW dextran that meets the limitations of the claims.

The claims remain rejected.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andriae M. Holt whose telephone number is (571)272-9328. The examiner can normally be reached on 7:00 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richter Johann can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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